Erasmus MC
Universitair Medisch Centrum Rotterdam

TCTAP 2014, Session: DES Failure: Why and How?

The Imaging Evidences: Time-related Differences in Restenosis

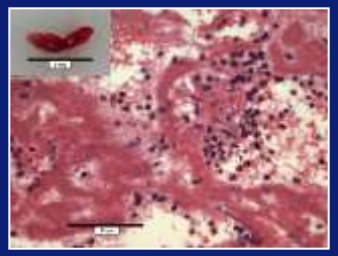
E. Regar
Thoraxcenter
Erasmus Medical Center
Rotterdam, NL

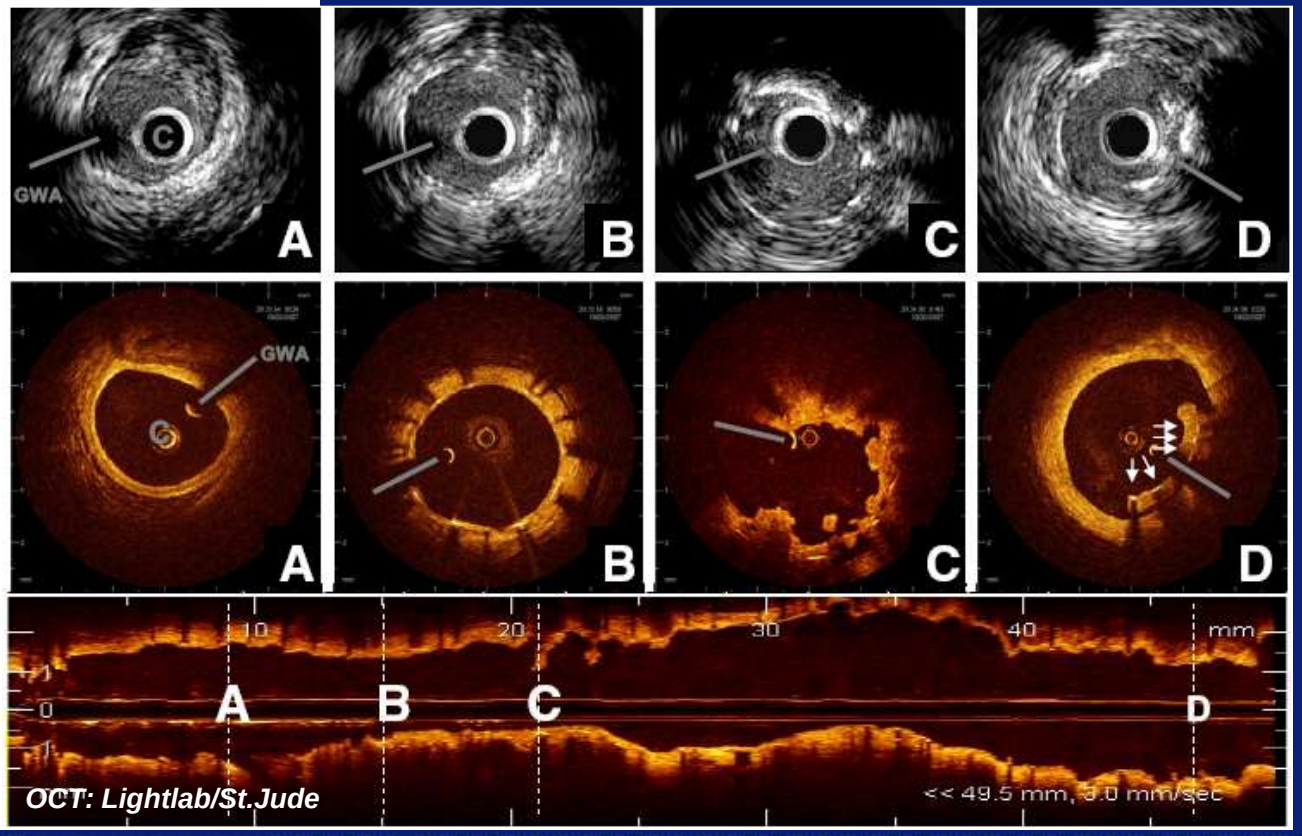
Mechanisms of Stent Failure: Uncovered & Malapposed Struts

IMAGES IN INTERVENTION

Optical Coherence Tomography Findings in Very Late (4 Years) Paclitaxel-Eluting Stent Thrombosis

Arend F. L. Schinkel, MD, PhD,* Peter Barlis, MD,* Heleen M. M
Patrick W. Serruys, MD, PhD, FACC,* Evelyn Regar, MD, PhD
Rotterdam, the Netherlands



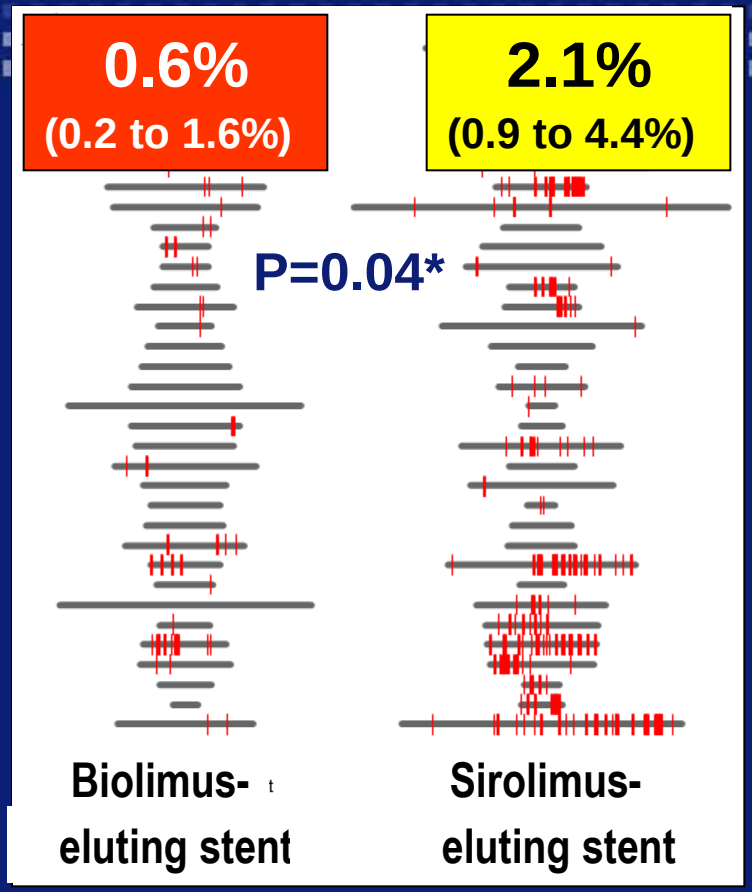


Schinkel, Regar et al. JACC: Cardiovasc Interv 2008

Mechanisms of Stent Failure: Uncovered & Malapposed Struts

Low incidence !

at 9m FUP



LEADERS Trial

L*imus* ***E****luted from* ***A*** ***D****urable versus* ***ER****odable* ***S****tent Coating*

Graphical representation of stent coverage in lesions

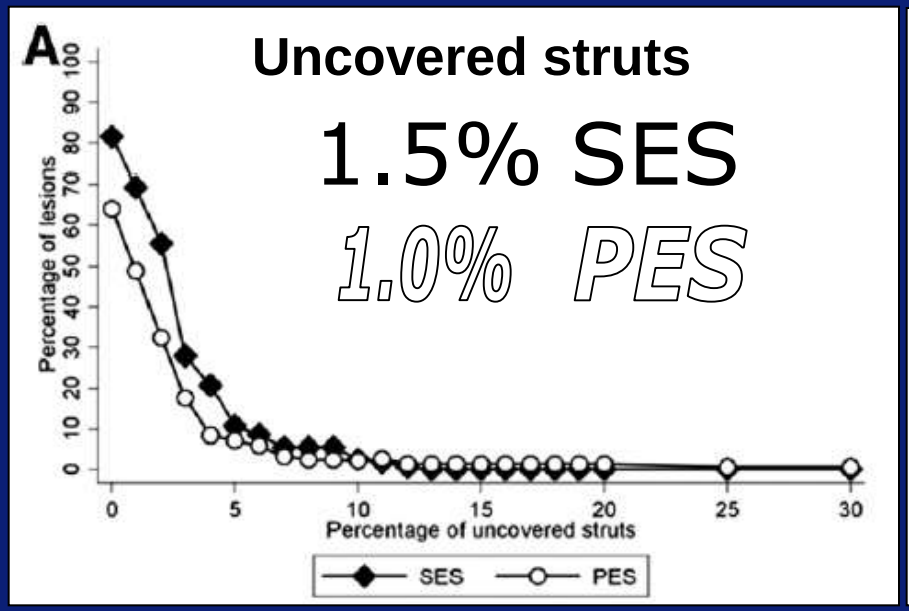
Barlis, Regar et al. Eur Heart J 2009

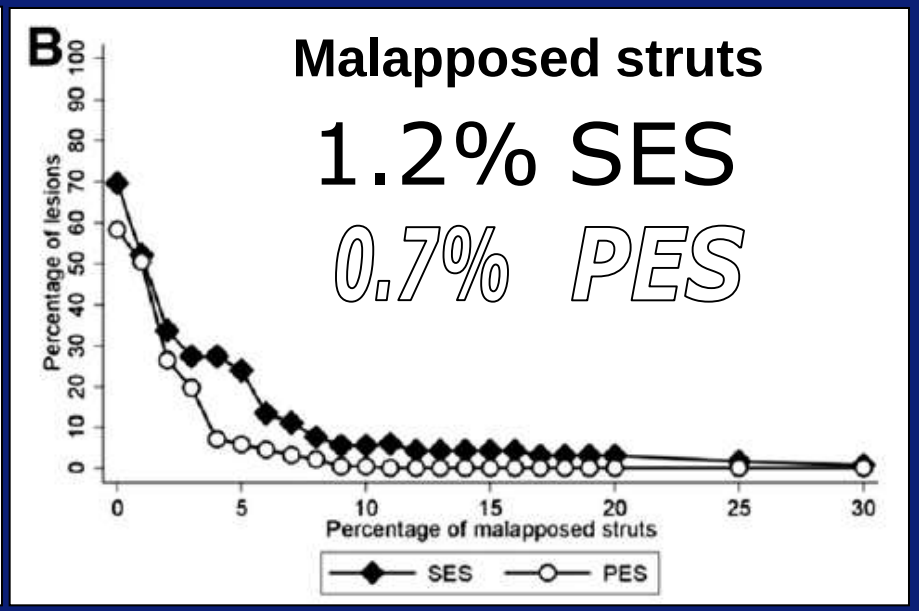
Mechanisms of Stent Failure: Uncovered & Malapposed Struts

Erasmus MC Zafung

Low incidence !

at 5y FUP





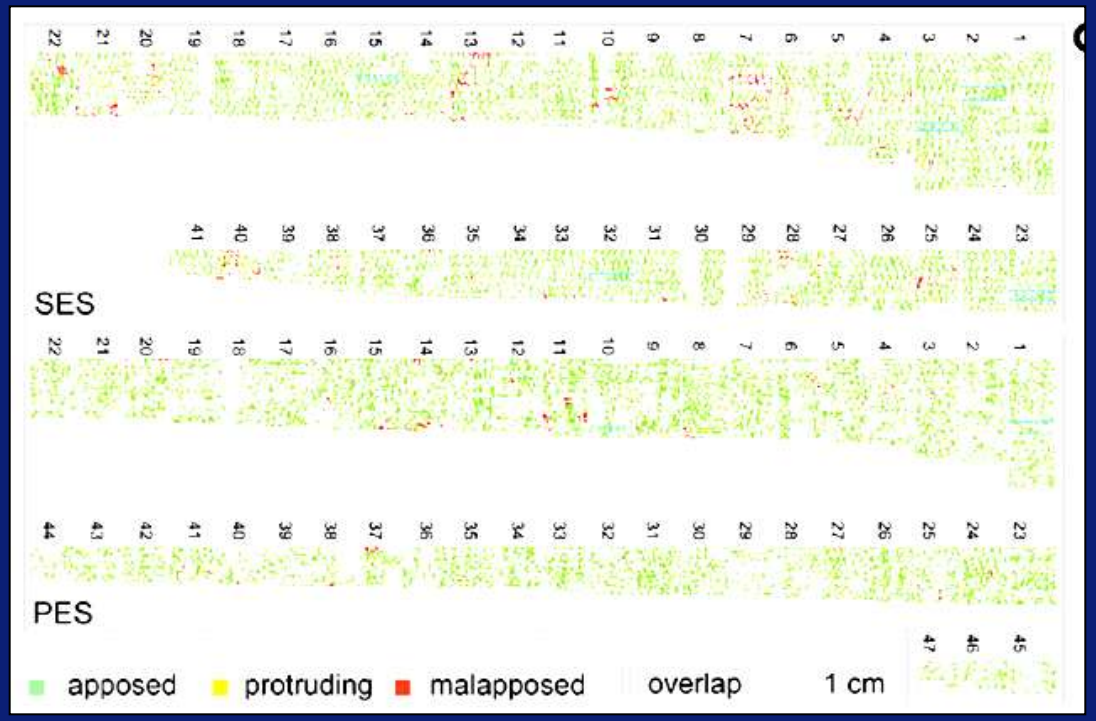
SIRTAX late OCT trial; N=88 pts; event-free; FUP 5y

Räber et al. JACC: Cardiovasc Interv 2012

Mechanisms of Stent Failure: Uncovered & Malapposed Struts

Low incidence !

Clustering in few patients

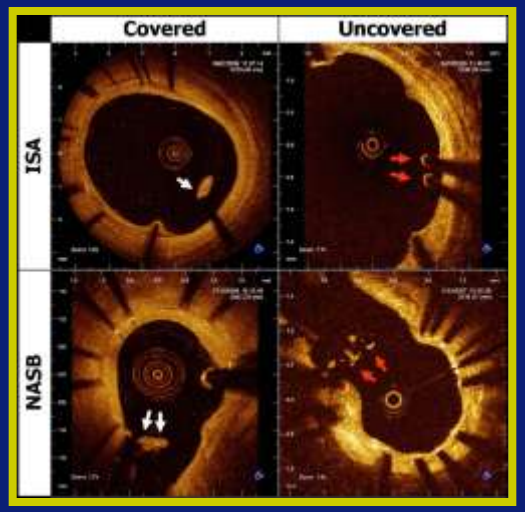


SIRTAX late OCT trial; N=88 pts; event-free; FUP 5y

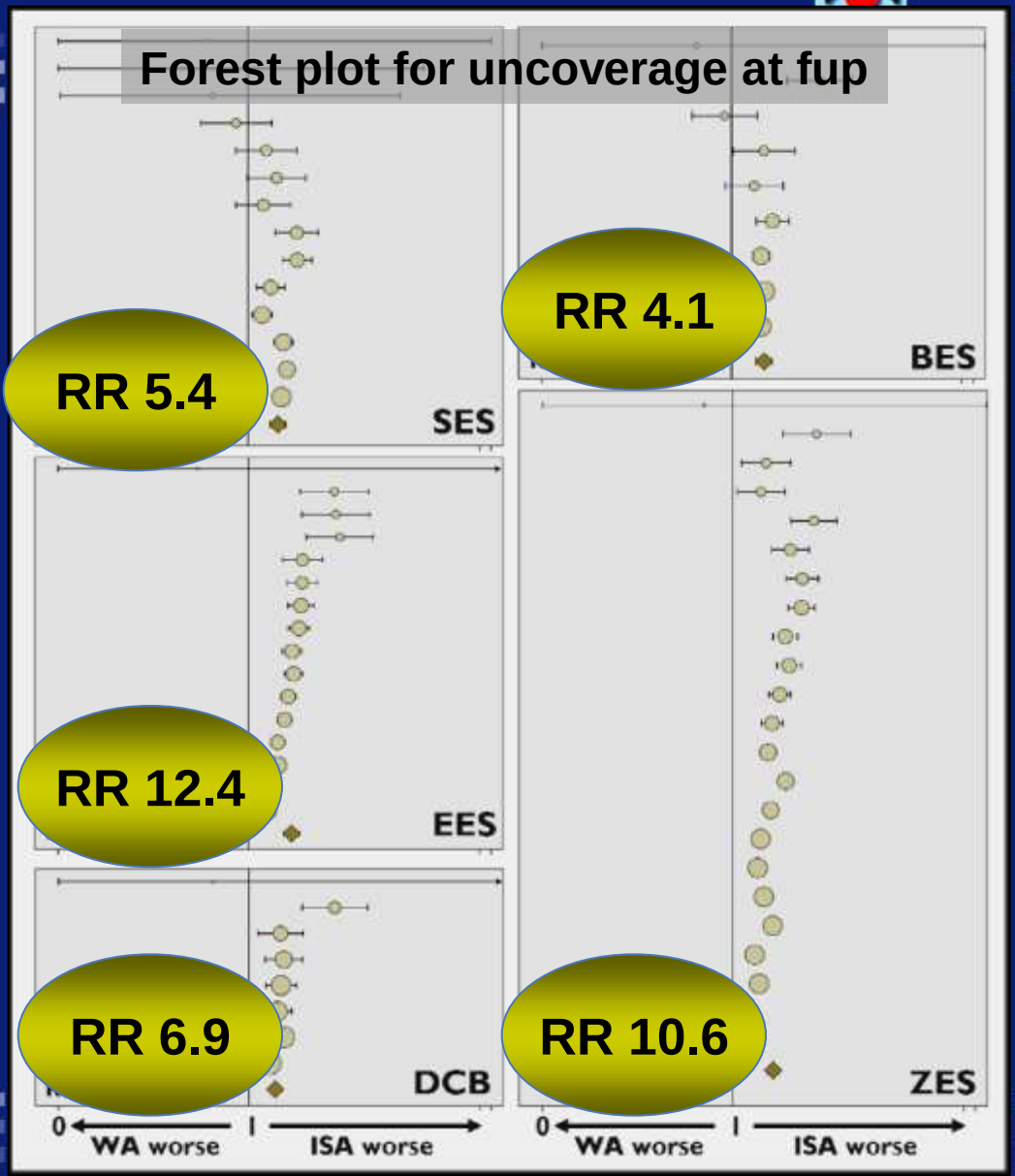
Räber et al. JACC: Cardiovasc Interv 2012

Mechanisms of Stent Failure: Uncovered & Malapposed Struts

Interaction: Malapposed struts are at increased risk for uncoverage



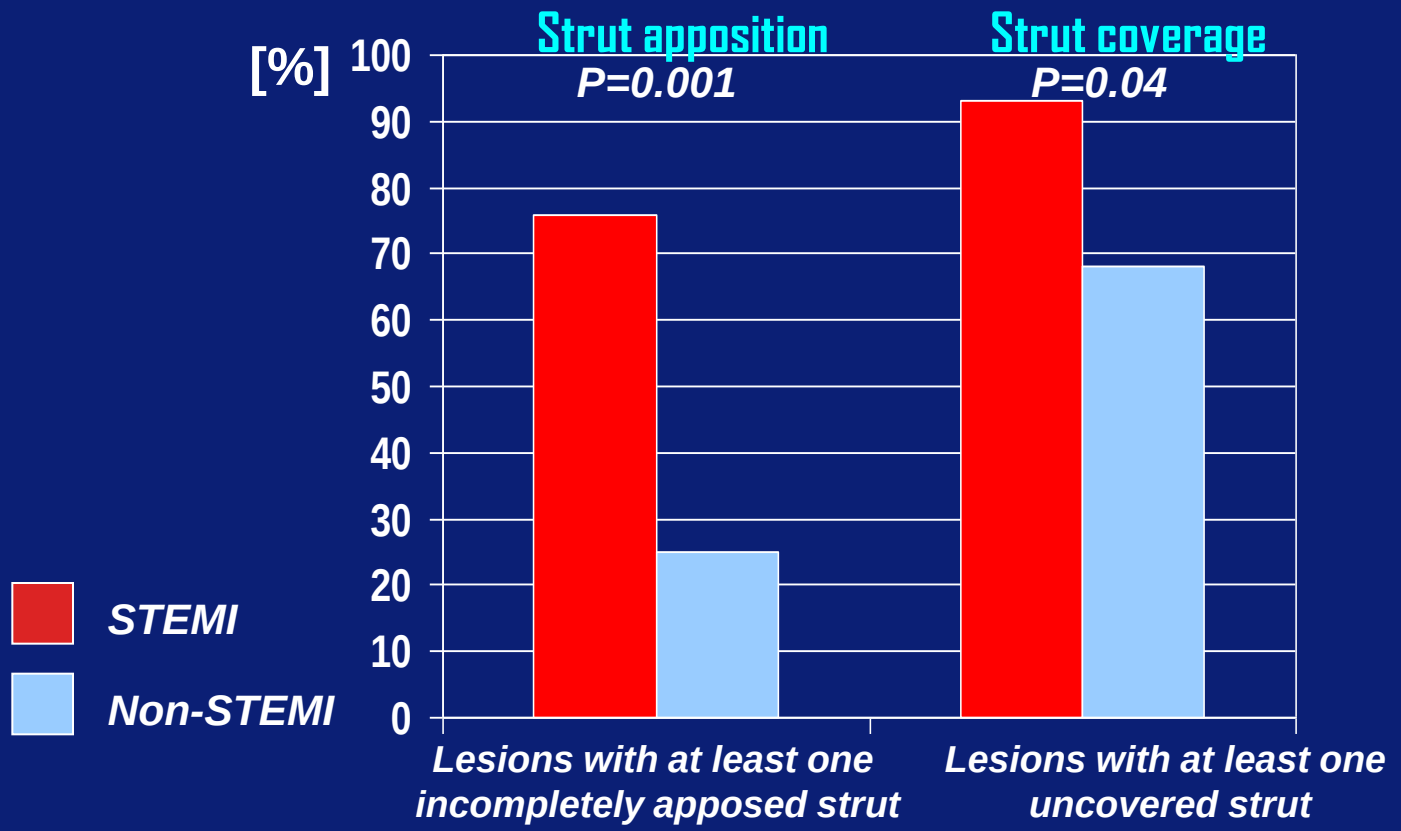
ISA: incomplete strut apposition
WA: well-apposed struts



Gutierrez, Regar et al. Circulation 2011

Mechanisms of Stent Failure: Uncovered & Malapposed Struts

Higher incidence in patients treated for STEMI



Gonzalo, Regar et al. JACC: Cardiovascular Interv. 2009;2(5):445-52.

Mechanisms of Stent Failure: Uncovered & Malapposed Struts

Higher incidence in pts with Late Stent Thrombosis!

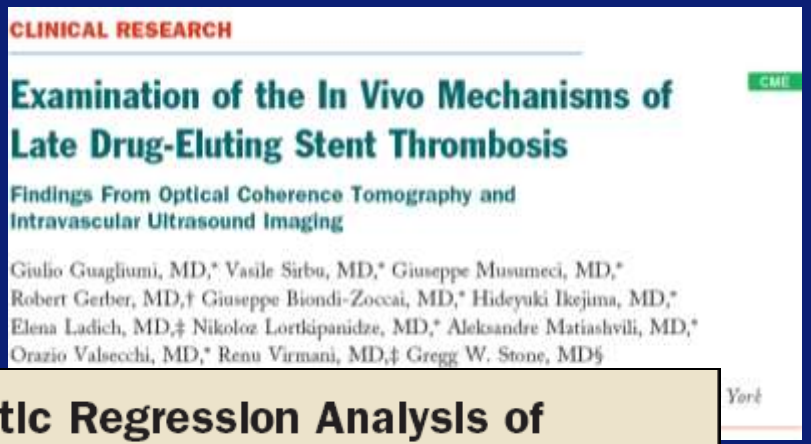
Table 2. Optical Coherence Tomography Imaging Measurements

	ST	Control	
Cross-section level analysis			
Analyzed cross-sections/patient, n	27 ± 12	30 ± 13	0.47
Struts analyzed/cross-section, n	6.78 ± 1.22	6.74 ± 1.41	0.93
Frequency of cross-sections with uncovered struts, %	33.30 (11.82–53.00)	0.00 (0.00–7.80)	0.003
Frequency of cross-sections with >30% uncovered struts, %	21.59 (0.00–43.70)	0.00 (0.00–6.09)	0.002
Maximum length of segments with uncovered struts, mm	3.30 (1.35–4.13)	0.90 (0.00–1.55)	<0.001
Maximum length of segments with malapposed struts, mm	1.40 (0.68–1.93)	0.00 (0.00–0.00)	0.001
Maximum malapposition distance, mm	0.35 (0.00–0.75)	0.00 (0.00–0.62)	0.002
Area of malapposition, mm^2	1.02 (0.00–1.92)	0.00 (0.00–0.32)	0.002
Minimum stent area, mm^2	5.04 ± 1.23	5.50 ± 1.27	0.26
Mean stent area, mm^2	7.24 ± 0.97	7.69 ± 1.61	0.20
Mean neointimal area, mm^2	1.57 ± 0.68	1.68 ± 0.71	0.41
Uncovered struts/pts	**12.2%**	**4.2%**	**0.001**
Malapposed struts/pts	**4.6%**	**1.8%**	**0.001**
Number of malapposed struts/patient	10.00 (2.25–21.75)	4.00 (0.00–7.00)	0.02
Frequency of malapposed struts/patient, %	4.60 (1.85–7.19)	1.81 (0.00–2.99)	0.001
Neointimal thickness of covered struts, mm	0.23 ± 0.15	0.17 ± 0.09	0.28

Guagliumi et al. JACC: Cardiovascular Interv. 2012

OCT Predictor of Late DES Thrombosis

Uncovered struts segment length



CLINICAL RESEARCH

CME

Examination of the In Vivo Mechanisms of Late Drug-Eluting Stent Thrombosis

Findings From Optical Coherence Tomography and Intravascular Ultrasound Imaging

Giulio Guagliumi, MD,* Vasile Sirbu, MD,* Giuseppe Musumeci, MD,*
Robert Gerber, MD,† Giuseppe Biondi-Zoccai, MD,* Hideyuki Ikejima, MD,*
Elena Ladich, MD,‡ Nikoloz Lortkipanidze, MD,* Aleksandre Matiashvili, MD,*
Orazio Valsecchi, MD,* Renu Virmani, MD,‡ Gregg W. Stone, MD§

York

Table 4: Exploratory Multivariable Logistic Regression Analysis of Late Stent Thrombosis

Variable	OR (95% CI)	p Value
Maximum length of segments with uncovered struts at OCT, mm	2.45 (1.27–4.73)	0.007
Remodeling index at IVUS*	1.05 (1.01–1.11)	0.019

Guagliumi et al. JACC: Cardiovascular Interv. 2012

Mechanisms of Stent Failure: Restenosis

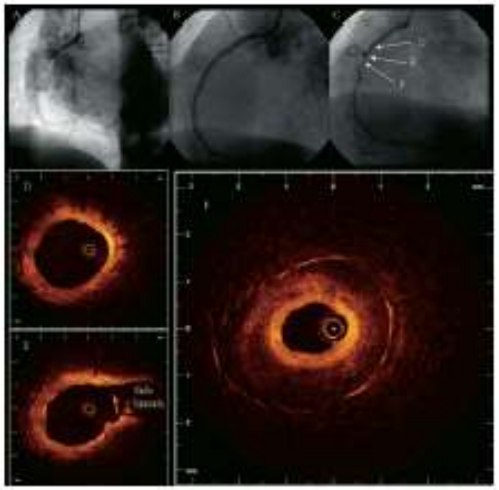
EuroIntervention

Paclitaxel-eluting stent restenosis shows three-layer appearance by optical coherence tomography

Shuzou Tanimoto, MD; Jiro Aoki, MD; Patrick W. Serruys, MD, PhD; Evelyn Regar*, MD, PhD

Thoraxcenter, Erasmus Medical Center, Rotterdam, The Netherlands.

A 73-year-old woman with hypertension, hyperlipidemia and positive familial history of coronary artery disease presented with Canadian Cardiovascular Society class III angina and underwent coronary angiography, which showed a chronic occluded right coronary artery (Panel A). The vessel was recanalized and treated with three paclitaxel-eluting stents (TAXUS®, Boston Scientific: 3.5 x 32 mm distally, 3.5 x 28 mm in the middle part, 3.5 x 12 mm proximally). Postintervention coronary angiography showed a good result (Panel B). Twelve-month follow-up angiography revealed focal in-stent restenosis (Panel C). Intracoronary optical coherence tomography (OCT: LightLabImaging™, Boston, MA, USA) pullback displayed well-expanded stents covered with a thin, homogenous, highly reflective neointimal layer (Panel D, E). In contrast, the narrowest lesion site (minimal lumen area 1.1 mm²; stent area 9.0 mm²) showed a three-layer appearance of the neointima (Panel F). The inner luminal layer appeared concentric, homogenous and signal-rich (maximal thickness 0.27 mm). A second layer consisting of a low-reflective area with poorly delineated borders followed. The third layer was in direct contact with the stent struts and revealed only minimal signal intensity. These signal-poor areas (maximal thickness 1.18 mm) might represent acellular fibrinoid deposition that has been well described in experimental studies. The patient was re-treated with repeat paclitaxel-eluting stent implantation. OCT is an analogue of intravascular ultrasound with an ultra-high resolution (10 µm) superior to any current available imaging modalities. This imaging device may be useful in visualizing neointimal growth in drug-eluting stents and improve our understanding of its underlying physiopathology in the future.

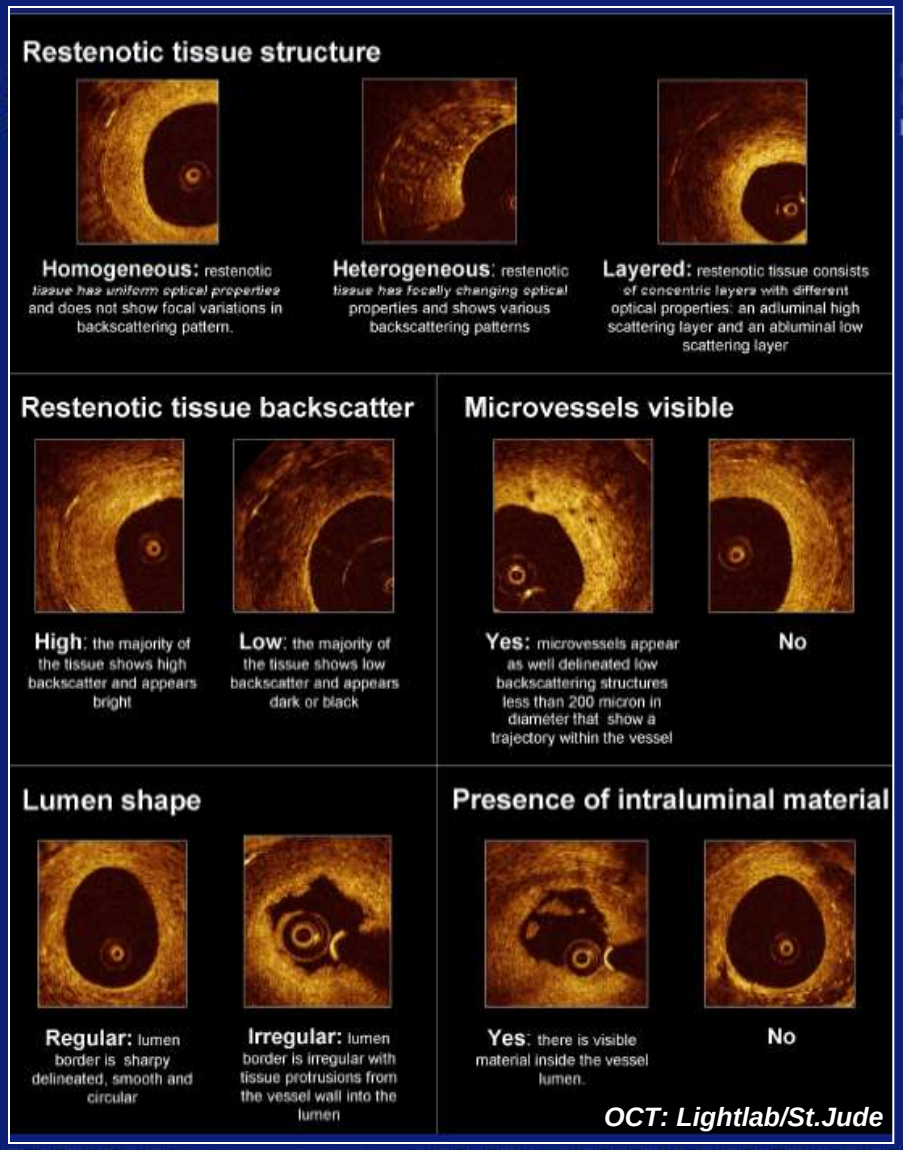


OCT: Lightlab/St.Jude

Tanimoto, Regar et al. Eurointervention 2006

Mechanisms of Stent Failure: Restenosis

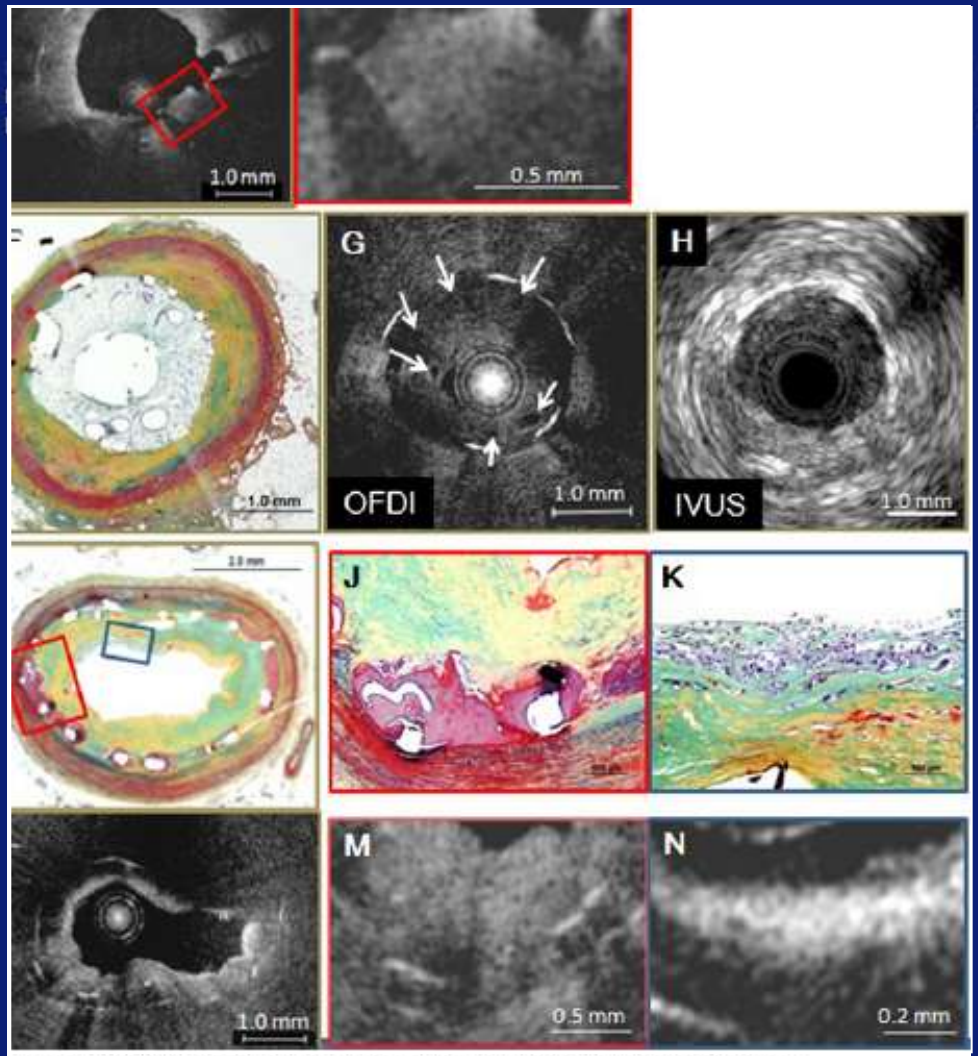
In 2009: OCT analysis descriptive



Gonzalo, Regar et al. Am Heart J 2009

Mechanisms of Stent Failure: Restenosis

In 2012: OCT validation against histology



How Do OCT and IVUS Compare to Histology in Coronary Atherosclerosis and Stenting?

Fumiyuki Otsuka · Masataka Nakano · Frank D. Kolodgie · Renu Virmani

Otsuka et al. Curr Cardiovas Img Rep 2012

Mechanisms of Stent Failure: Restenosis

Erasmus MC

In 2012: OCT terminology established

European Heart Journal
doi:10.1093/eurheartj/ehp433

REVIEW

Expert review document on methodology, te… al applications of optical co… : physical principles, m… acquisition, and clinical ap… ent of coronary arteries an…

Fra… S. Mintz[3], Eloisa Arbustini[4], Carlo Di Mario[5], Ik-Kyung Jang[6], Takashi Akasaka[7], Marco Costa[8], Giulio Guagliumi[9], Eberhard G… Expert's O…

European Heart Journal
doi:10.1093/eurheartj/ehs095

CURRENT OPINION

Expert review document part 2: methodology, terminology and clinical applications of optical coherence tomography for the assessment of interventional procedures

Francesco Prati[1,2*], Giulio Guagliumi[3], Gary S. Mintz[4], Marco Costa[5], Evelyn Regar[6,7], Takashi Akasaka[8], Peter Barlis[9], Guillermo J. Tearney[10,11], Ik-Kyung Jang[12], Elosia Arbustini[13], Hiram G. Bezerra[5], Yukio Ozaki[14], Nico Bruining[6,7], Darius Dudek[15], Maria Radu[6,7], Andrejs Erglis[16], Pascale Motreff[17], Fernando Alfonso[18], Kostas Toutouzas[19], Nieves Gonzalo[20], Corrado Tamburino[21], Tom Adriaenssens[22], Fausto Pinto[23], Patrick W.J. Serruys[6,7], and Carlo Di Mario[24,25], for the Expert's OCT Review Document

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MINI-FOCUS ISSUE: OPTICAL COHERENCE TOMOGRAPHY

Clinical Research

Consensus Standards for Acquisition, Measurement, and Reporting of Intravascular Optical Coherence Tomography Studies

A Report From the International Working Group for Intravascular Optical Coherence Tomography Standardization and Validation

Guillermo J. Tearney, MD, PHD, *Writing Committee Co-Chair*,*
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Nico Bruining, PHD, Jin-man Cho, MD, PHD, Saqib Chowdhary, PHD, Marco A. Costa, MD, PHD,
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Yasuhiro Honda, MD, Fumiaki Ikeno, MD, Masanori Kawasaki, MD, Janusz Kochman, MD, PHD,
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Akiko Maehara, MD, Olivia Manfrini, MD, Gary S. Mintz, MD, Kyiouchi Mizuno, MD,
Marie-angéle Morel, MD, Seemantini Nadkarni, PHD, Hiroyuki Okura, MD, Hiromasa Otake, MD,
Arkadiusz Pietrasik, MD, Francesco Prati, MD, Lorenz Räber, MD, Maria D. Radu, MD,
Johannes Rieber, MD, Maria Riga, MD, Andrew Rollins, PHD, Mireille Rosenberg, PHD, Vasile Sirbu, MD,
Patrick W. J. C. Serruys, MD, PHD, Kenei Shimada, MD, Toshiro Shinke, MD, Junya Shite, MD,
Eliot Siegel, MD, Shinjo Sonada, MD, Melissa Suter, PHD, Shigeho Takarada, MD, PHD,
Atsushi Tanaka, MD, PHD, Mitsuyasu Terashima, MD, Thim Troels, MD, PHD, Shiro Uemura, MD, PHD,
Giovanni J. Ughi, PHD, Heleen M.M. van Beusekom, PHD, Antonius F.W. van der Steen, PHD,
Gerrit-Ann van Es, PHD, Gijs van Soest, PHD, Renu Virmani, MD, Sergio Waxman, MD,
Neil J. Weissman, MD, Giora Weisz, MD

Boston, Massachusetts; Rotterdam, the Netherlands; and Wakayama, Japan

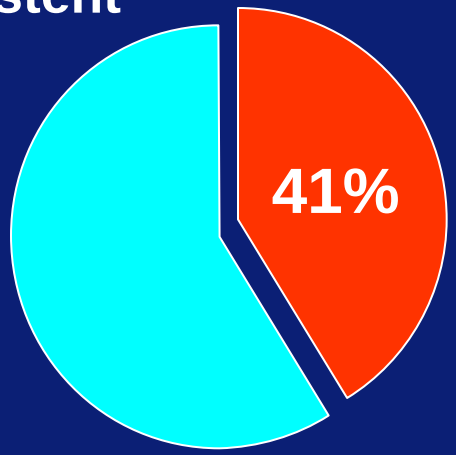
EHJ 2010 & 2012

J Am Coll Cardiol. 2012

Mechanisms of Stent Failure: Neoatherosclerosis

High incidence

Incidence of lipid laden plaque inside the stent



Development of lipid-rich plaque inside bare metal stent: possible mechanism of late stent thrombosis? An optical coherence tomography study

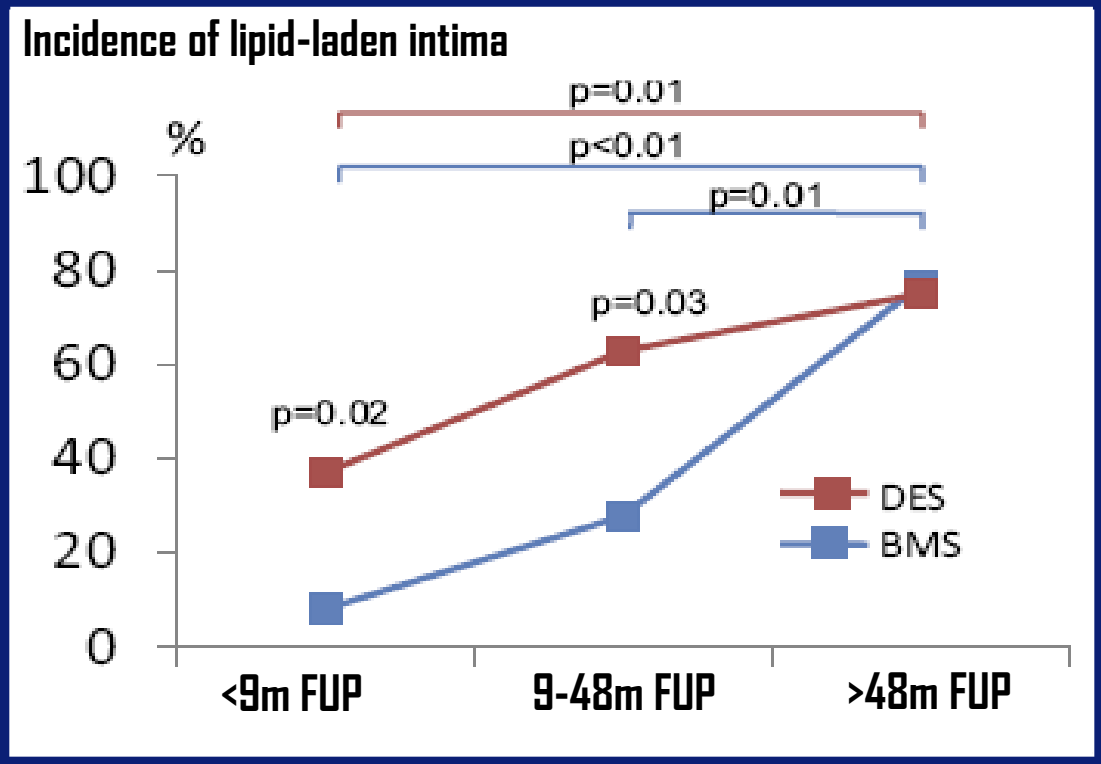
Jingbo Hou,[1] Hai Qi,[1] Maomao Zhang,[1] Lijia Ma,[1] Huimin Liu,[1] Zhigang Han,[1] Lingbo Meng,[1] Shuang Yang,[1] Shaosong Zhang,[2] Bo Yu,[1] Ik-Kyung Jang[3]

N= 39 pts
with recurrent ischemia
FUP 6.5±1.3 years after BMS

Hou et al. Heart 2010

Mechanisms of Stent Failure: Neoatherosclerosis

High incidence
Earlier onset in DES than in BMS

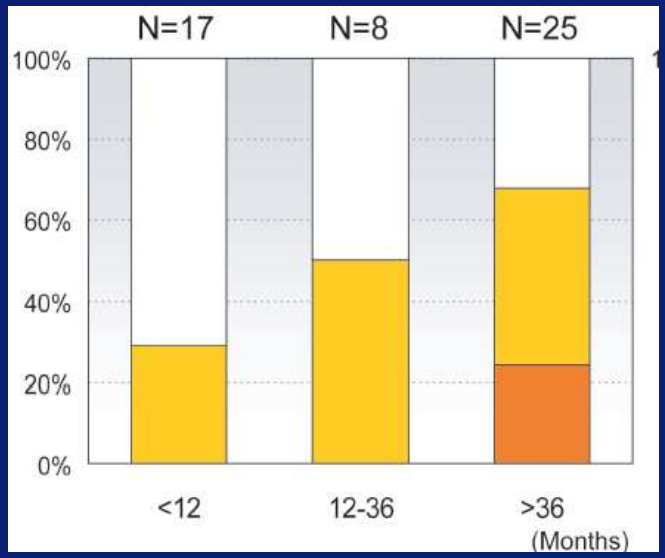


MGH OCT multicenter registry
N=124 pts with
neointimal thickness >100μm
in 3 consecutive cross sections

Yonetsu et al. Am J Cardiol 2012

Mechanisms of Stent Failure: Neoatherosclerosis

Increased TCFA

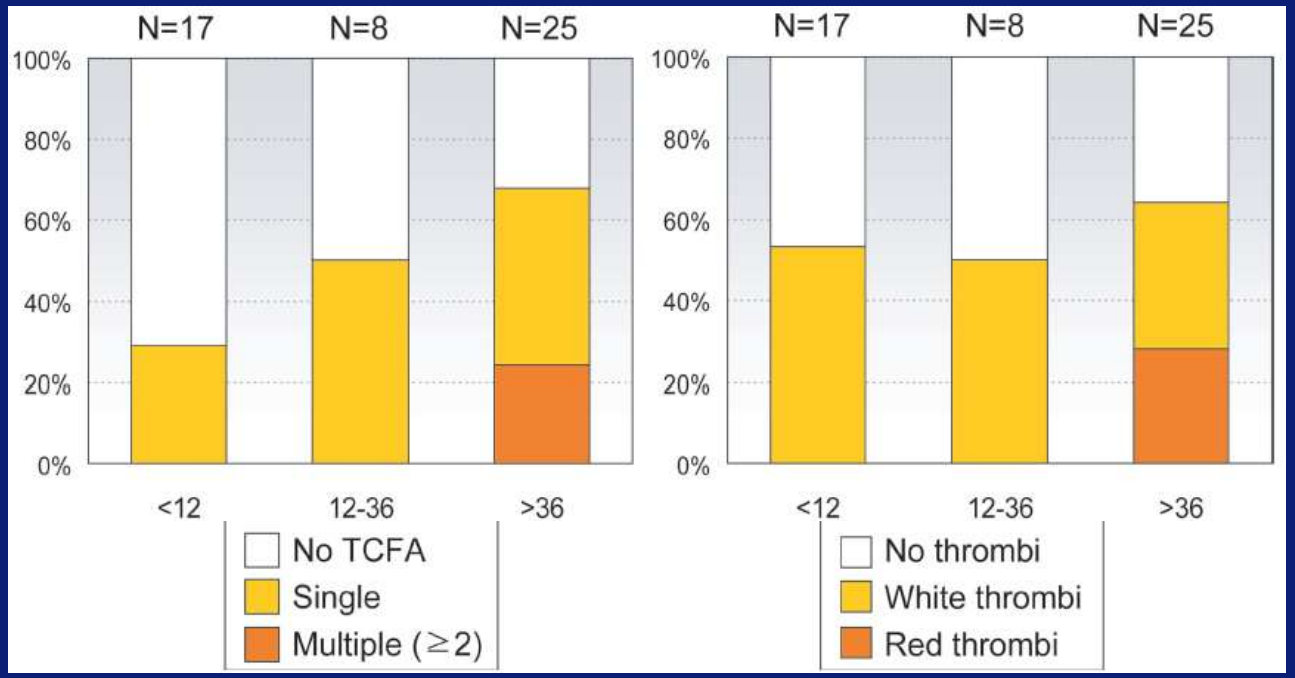


N= 54 pts with DES restenosis

Kang et al. Ciculation 2011

Mechanisms of Stent Failure: Neoatherosclerosis

Increased TCFA & Thrombi over time



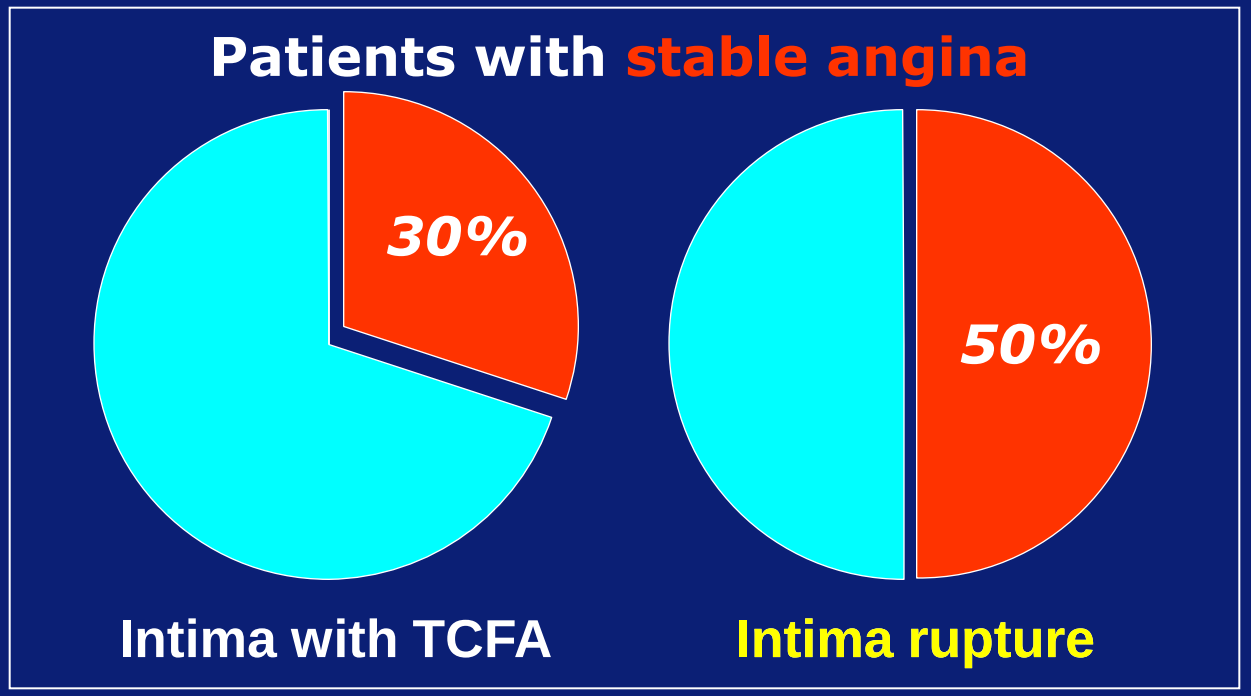
N= 54 pts with DES restenosis

Kang et al. Ciculation 2011

Mechanisms of Stent Failure: Neoatherosclerosis

Increased TCFA & Thrombi over time

Irrespective of clinical presentation

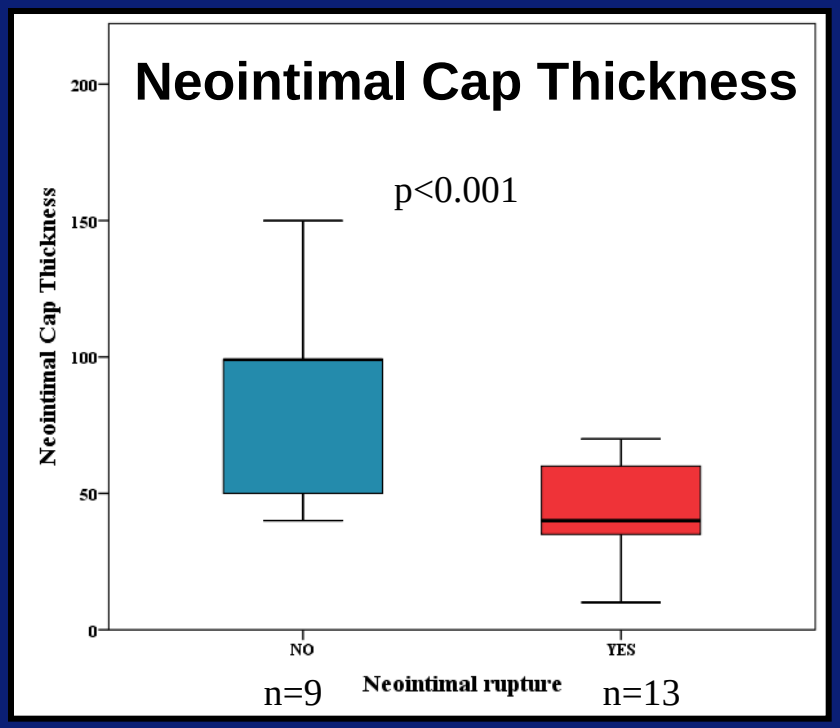


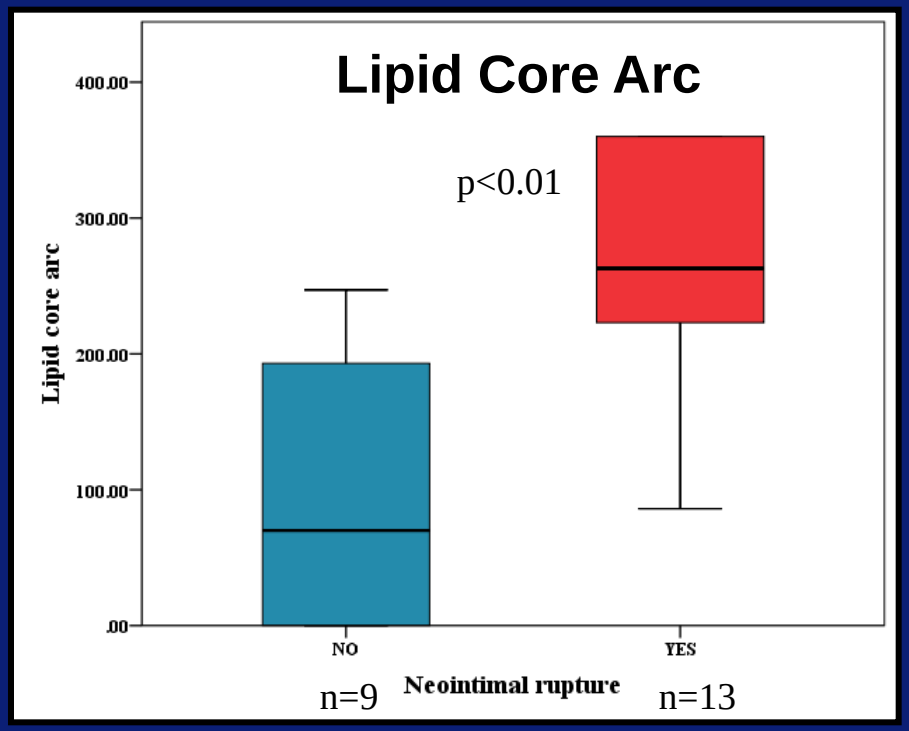
N= 54 pts with DES restenosis

Kang et al. Ciculation 2011

Mechanisms of Stent Failure: Neoatherosclerosis

Stents with neointimal rupture lower fibrous cap thickness & higher lipid content





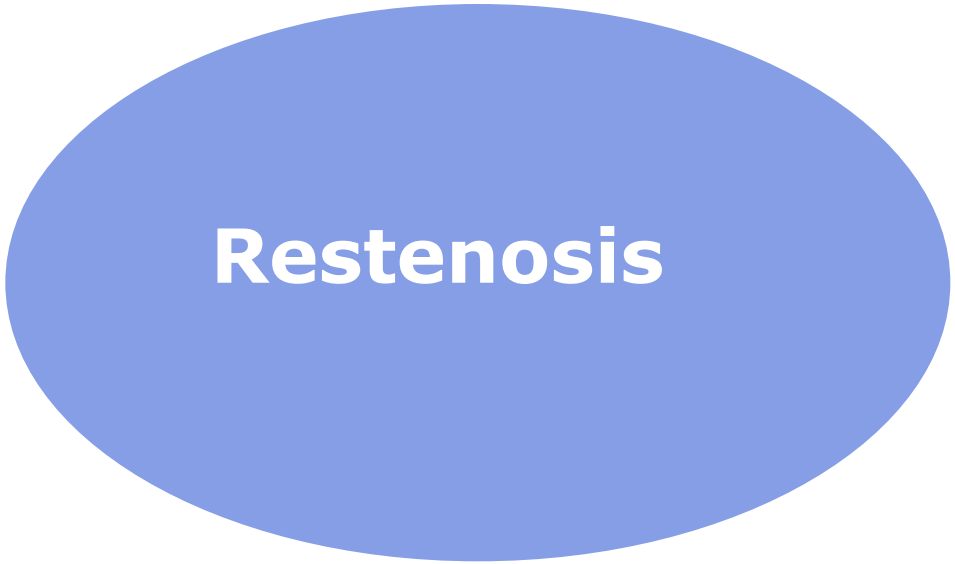
N=29 pts with very late stent thrombosis

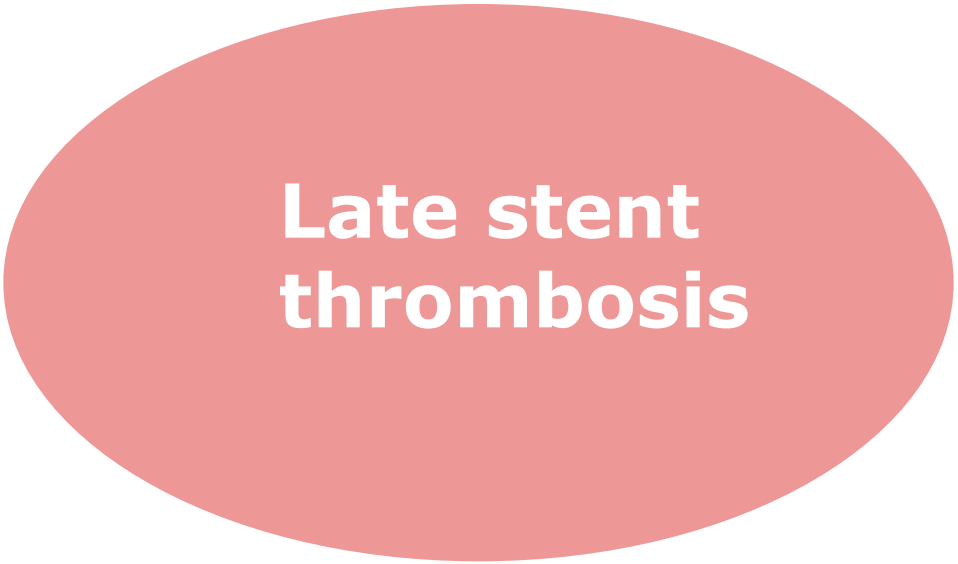
Karanasos, Regar et al. presented in part at ESC 2012

Karanasos, Regar et al. Poster at TCT 2012

Mechanisms of Stent Failure: Neoatherosclerosis

The link between restenosis & late stent thrombosis?



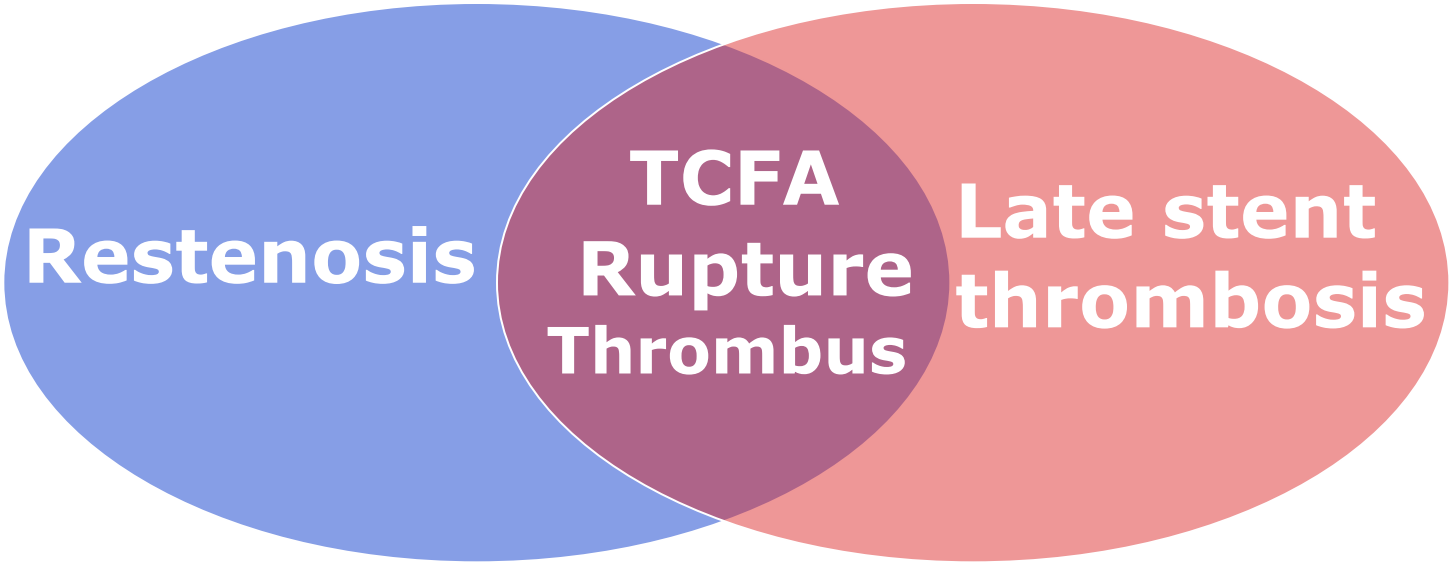


stable angina, "benign"

ACS, "life-threatening"

Mechanisms of Stent Failure: Neoatherosclerosis

The link between restenosis & late stent thrombosis?



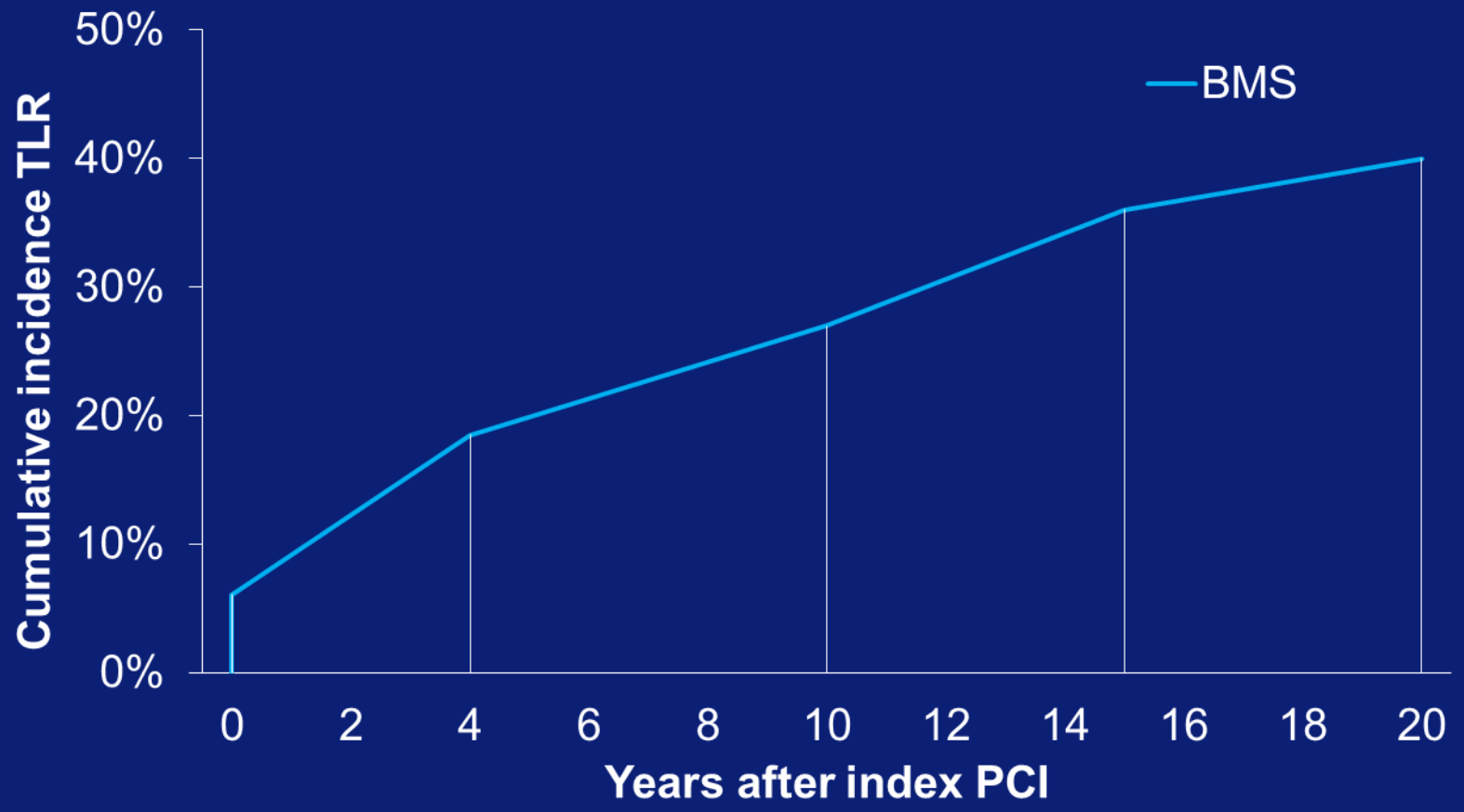
Neoatherosclerosis

Mechanisms of Stent Failure: Neoatherosclerosis

The link between restenosis & late stent thrombosis?

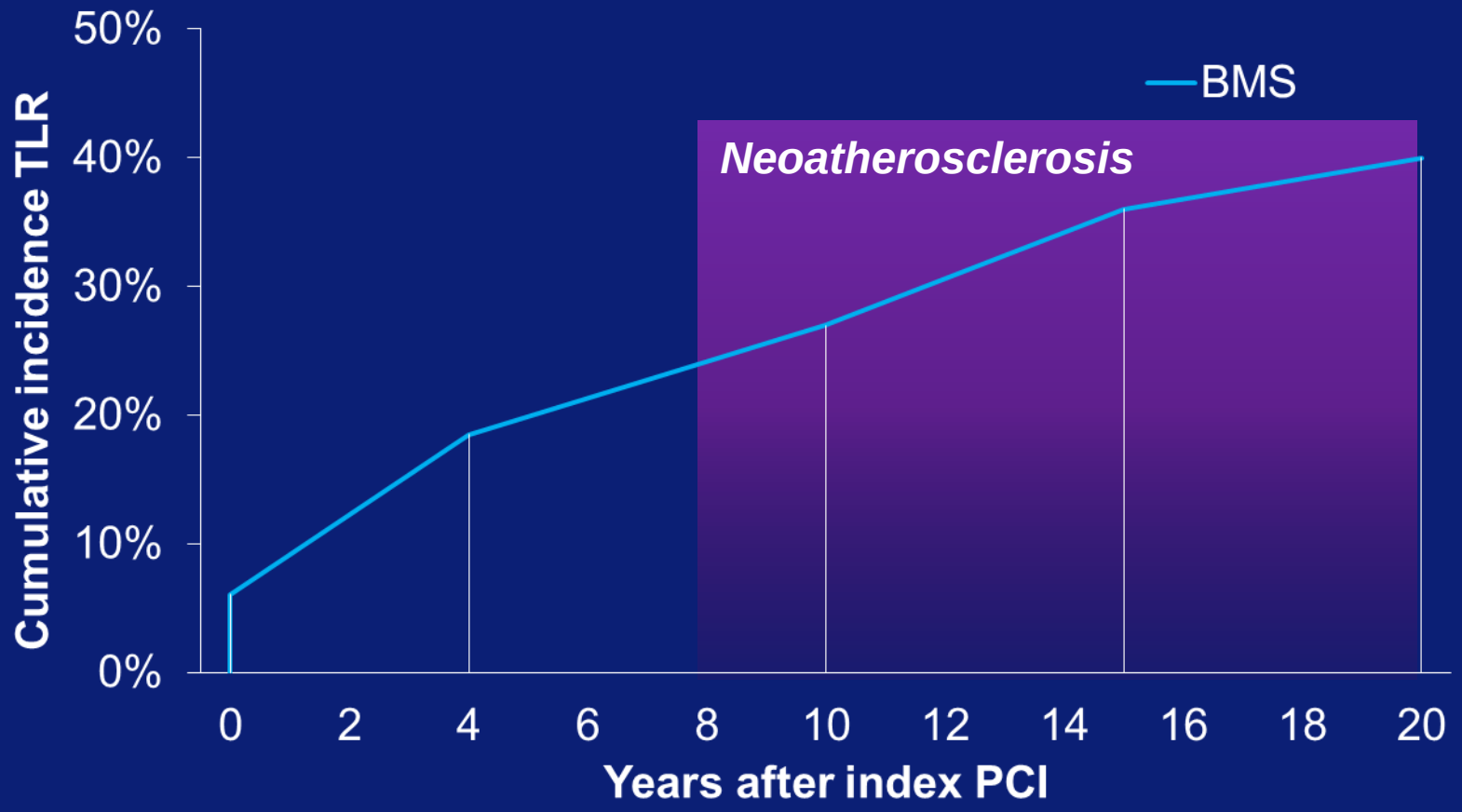
What's about timing?

Evidence of Ongoing Stent Failure



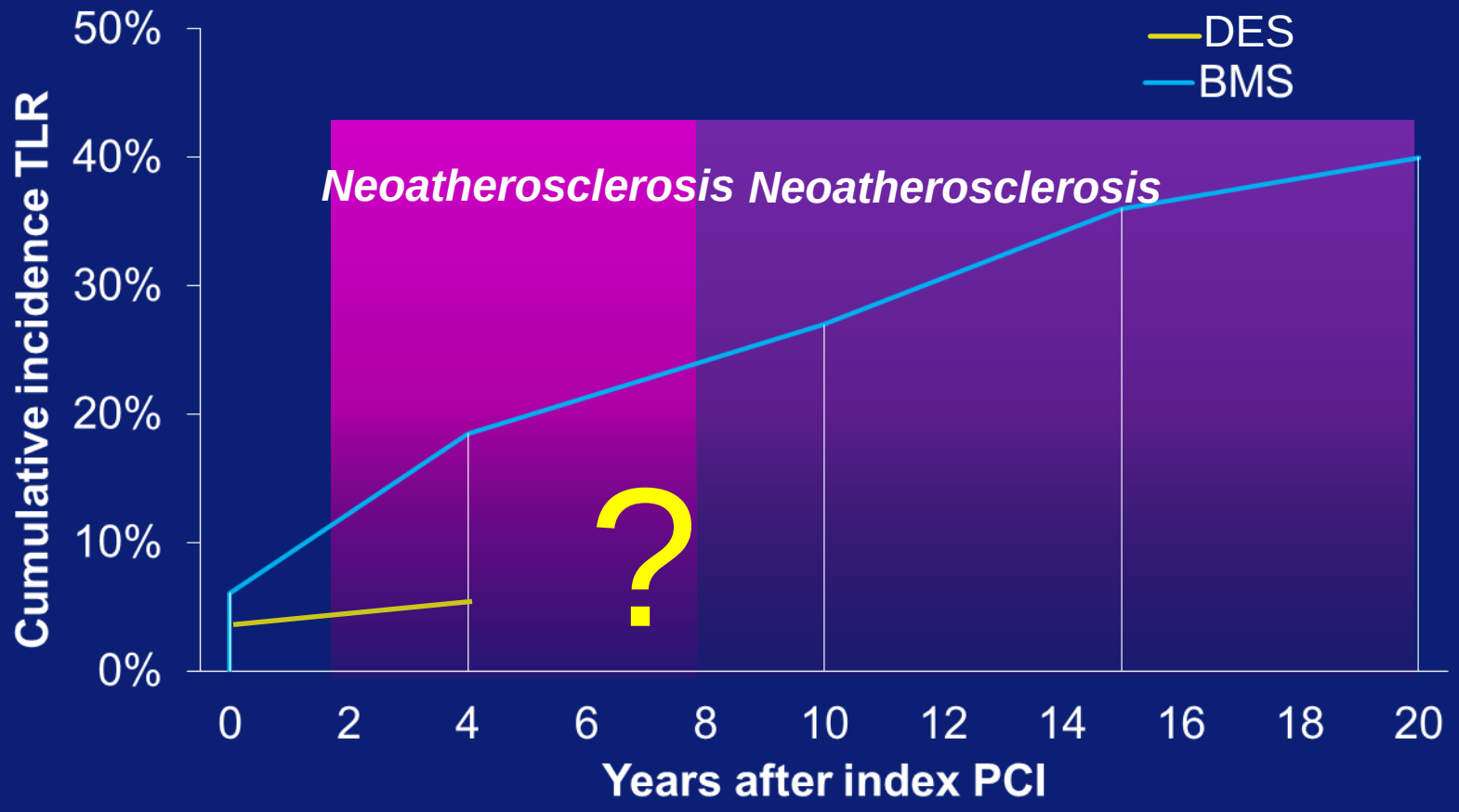
Yamaji K et al, Circ Cardiovasc Interv 2010

Evidence of Ongoing Stent Failure



Yamaji K et al, Circ Cardiovasc Interv 2010

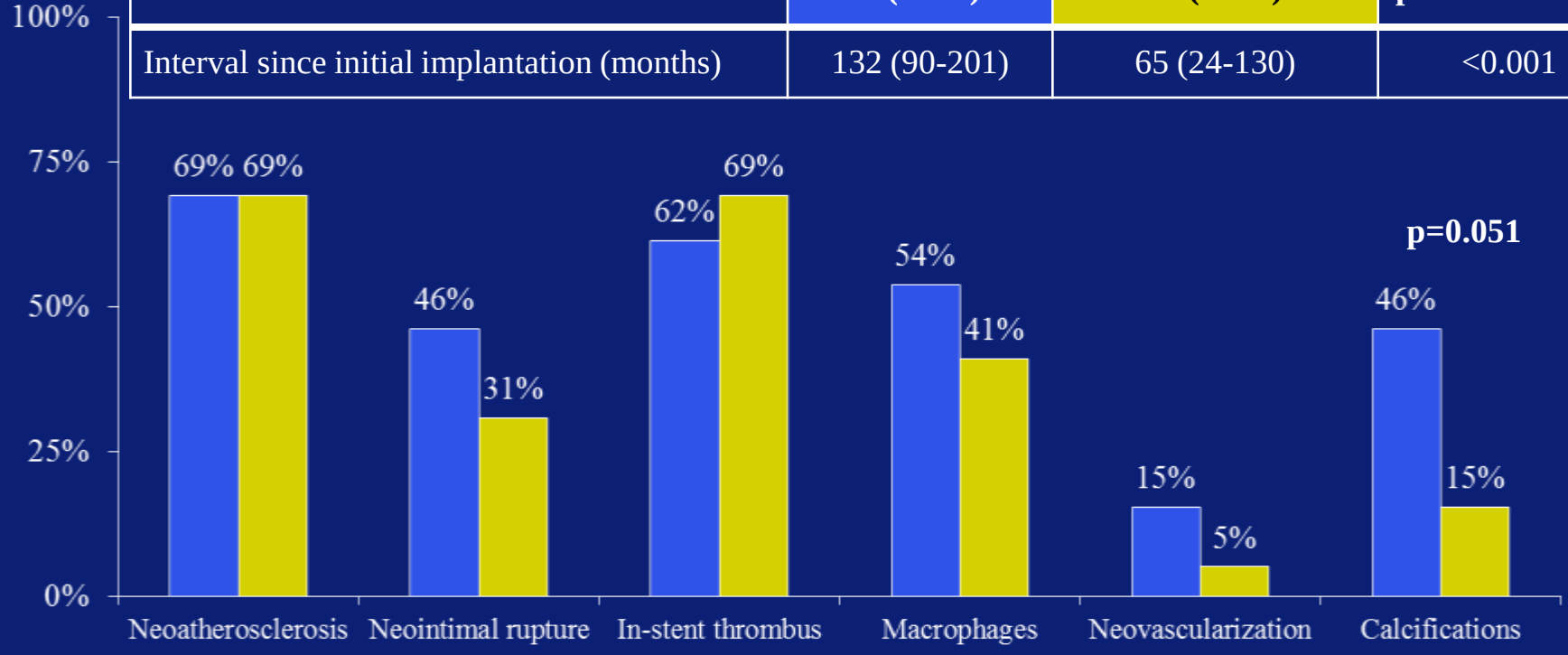
Evidence of Ongoing Stent Failure



Evidence of Ongoing Stent Failure Differences BMS vs DES 1st gen

Neoatherosclerosis in DES develops earlier with lower prevalence of calcifications

	BMS (n=13)	1st-DES (n=39)	p value
Interval since initial implantation (months)	132 (90-201)	65 (24-130)	<0.001



Kanarasos A et al SPIE 2014

Mechanisms and Predictors of Stent Thrombosis and Restenosis: Insights from OCT

Stent thrombosis and restenosis

- have various mechanisms (mechanical, pharmacological, biological)
- **both may be associated with coronary thrombosis**
- **neoatherosclerosis might be a common pathway**

Mechanisms and Predictors of Stent Thrombosis and Restenosis: Insights from OCT

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- **predictors are not well established yet**

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- **predictors are not well established yet**

- **develops much earlier in DES 1st gen than BMS**

Mechanisms and Predictors of Stent Thrombosis and Restenosis: Insights from OCT

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- both may be associated with coronary thrombosis
- neoatherosclerosis might be a common pathway

- predictors are not well established yet

- develops much earlier in DES 1st gen than BMS

Angiography fails to accurately visualize stent failure !

VLST:
Neoatherosclerosis & Rupture

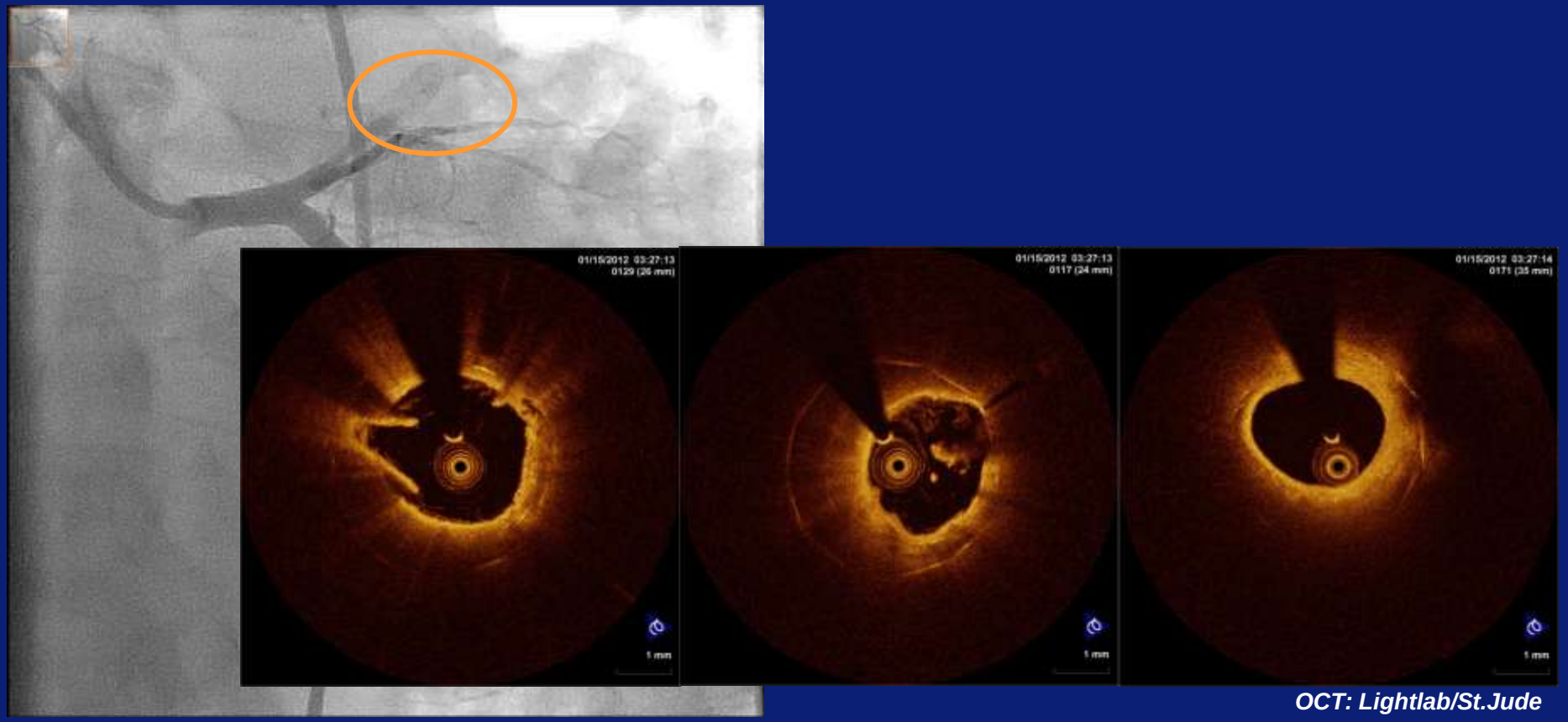
51y male presenting with anterior MI, 2004 PES implantation LAD. No CAD risk factors.

Co-registration: in cooperation with Medis, Leiden NL;

Tu, Regar et al. Int J Cardiovasc Imaging 2012

VLST:
Neoatherosclerosis & Rupture

51y male presenting with anterior MI, 2004 PES implantation LAD. No CAD risk factors.



OCT: Lightlab/St.Jude

VLST:
Mechanical Stent Problem

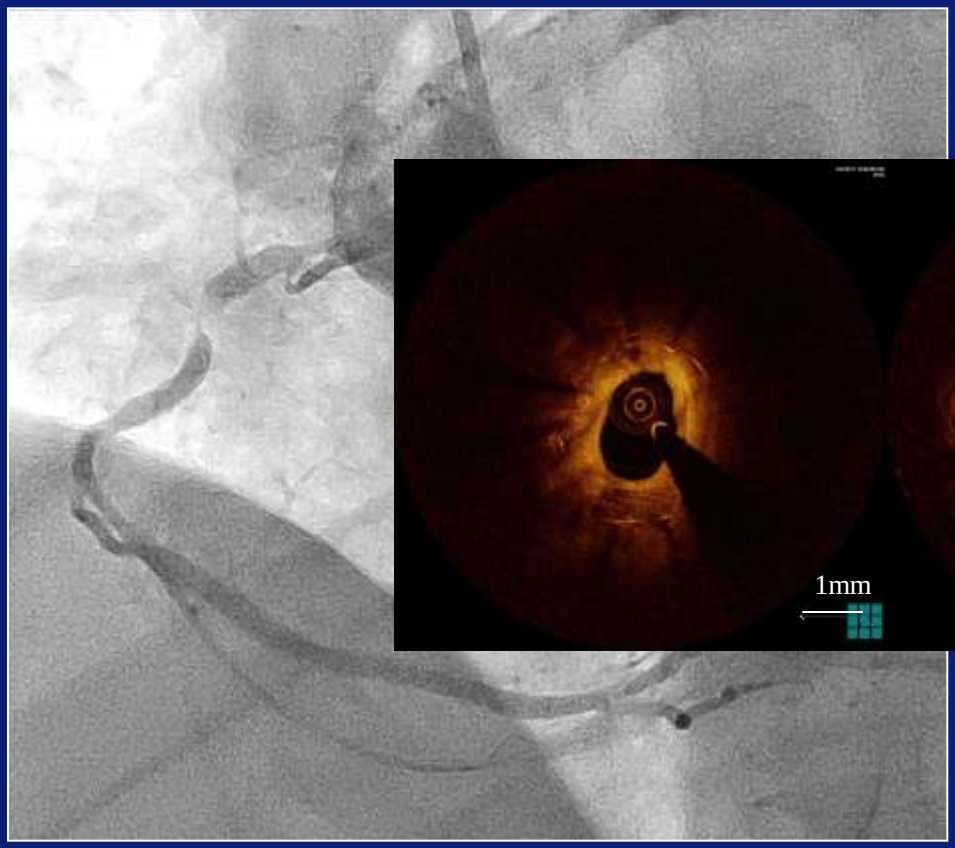
79 year old woman resuscitated after cardiac arrest. 2008 EES implantation. Pos. family history for CAD.

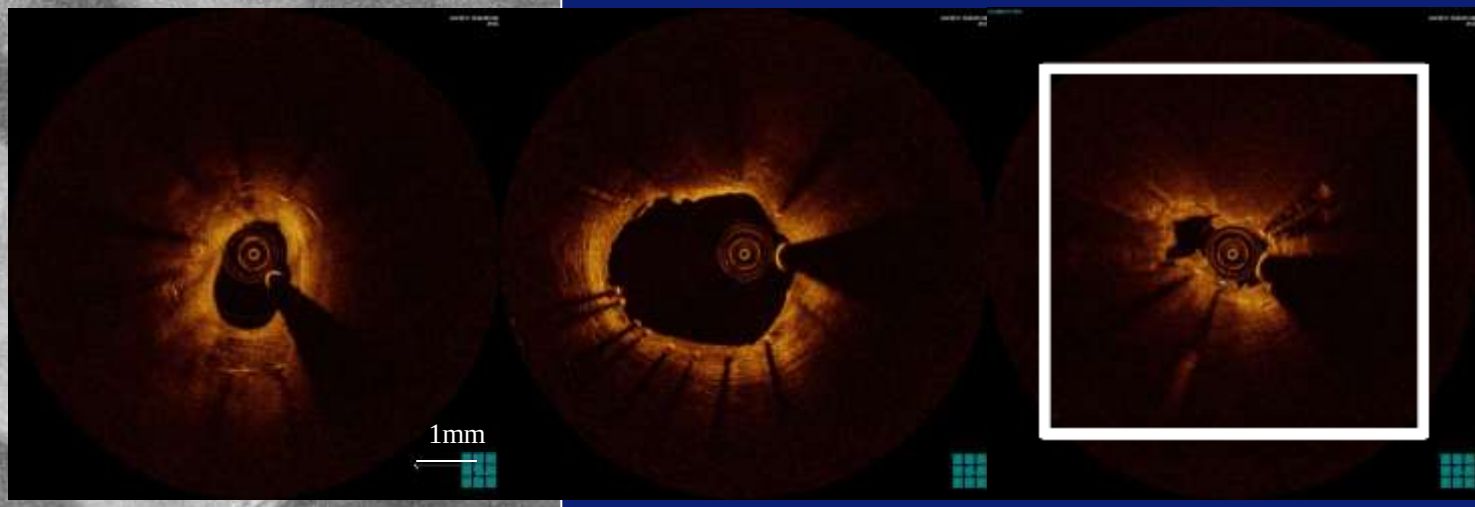
Co-registration: in cooperation with Medis, Leiden NL;

Tu, Regar et al. Int J Cardiovasc Imaging 2012

VLST:
Mechanical Stent Problem

79 year old woman resuscitated after cardiac arrest. 2008 EES implantation. Pos. family history for CAD.





OCT: Lightlab/St.Jude

Thank you for your attention!

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